IN THE UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

THE MEDICINES COMPANY,	)	
	)	
Plaintiff,	)	
	)	
v.	)	No. 11-cv-1285
	)	
MYLAN INC., MYLAN PHARMACEUTICALS INC., and BIONICHE PHARMA USA, LLC,	)	
	)	
Defendants.	)	

MEMORANDUM OPINION AND ORDER

AMY J. ST. EVE, District Court Judge:

This is a patent infringement action by The Medicines Company ("TMC") against Defendants Mylan, Inc., Mylan Pharmaceuticals Inc. and Bionche Pharma USA, LLC alleging infringement of United States Patent Nos. 7,582,727 (the "'727 patent") and 7,598,343 (the "'343 patent"). On December 16, 2013, the Court granted Defendants' motion for summary judgment of non-infringement with respect to the '343 patent and denied it with respect to the '727 patent. (*See* R. 309, Summ. Jdgmt. Op.) In the present motions, the parties seek to preclude each other from putting on evidence at trial that contradicts the Court's determinations on summary judgment. Specifically, Defendants move to preclude TMC's experts from (1) opining that Mylan's Abbreviated New Drug Application ("ANDA") uses an "efficient mixing" process and (2) offering opinions based on the assumption that Mylan's ANDA uses "efficient mixing," (*see* R. 331, Defs. Mot.), and TMC moves to preclude Defendants' fact and expert witnesses from testifying about "efficient" versus "inefficient mixing" conditions. (*See* R. 420, TMC Mot.) For the following reasons, the Court grants Defendants' motion in part, denies

it part, and denies it as moot in part. The Court denies TMC's motion in part and denies it as moot in part.

BACKGROUND

The '727 and the '343 patents pertain to pharmaceutical formulations of bivalirudin and the process of making bivalirudin. Bivalirudin is the active ingredient in TMC's Angiomax® drug product, an injectable anticoagulant used to prevent blood clotting during coronary procedures. TMC has sold Angiomax® since 2001.

The '727 and '343 patents have nearly identical specifications, and they share similar prosecution histories. The principal difference between the two patents is that the asserted claims in the '343 patent require the use of "efficient mixing" in manufacturing the claimed bivalirudin drug product, and the '727 patent claims do not. In fact, although the '727 patent's specification discusses the process by which the claimed pharmaceutical batches are made, the claims themselves contain no process limitations.

Before expiration of the patents-in-suit, Mylan submitted ANDA No. 202471 to the U.S. Food and Drug Administration ("FDA"), seeking approval to engage in the commercial manufacture, use, sale, offer for sale, and/or importation of a generic equivalent to Angiomax®. TMC filed suit, claiming that Mylan's ANDA infringes several claims of the '727 and '343 patents. On December 16, 2013, the Court granted Defendants summary judgment of non-infringement with respect to the '343 patent. (*See* Summ. Jdgmt. Op.) The Court, however, denied Defendants' motion for summary judgment with respect to the '727 patent.

Two of the Court's determinations on summary judgment relate to the motions currently before the Court. First, the Court held on summary judgment that Mylan's ANDA does not teach "efficient mixing." The Court has construed the term "efficient mixing" to mean that "[a]

pH-adjusting solution and the [bivalirudin] solution are mixed not using inefficient mixing conditions such as described in Example 4" of the patent specification. (*See* R. 119, Claim Construction Op. at 30.) After comparing the compounding process described in Mylan's ANDA to the inefficient mixing conditions described in Example 4 of the specification, the Court found that Mylan's ANDA process was even *more inefficient* than Example 4's inefficient mixing conditions. Accordingly, the Court held that Mylan's ANDA does not teach "efficient mixing" and, therefore, does not infringe the asserted claims in the '343 patent.

Second, the Court held that the asserted claims in the '727 patent do not contain an "efficient mixing" limitation or, for that matter, any process limitations whatsoever. In making this determination, the Court found it significant that, although the '343 and '727 patent specifications are nearly identical, the process limitations present in the '343 patent claims are notably absent from the '727 patent claims. Because the '727 patent claims do not contain any process limitations, the Court held that the '727 patent is a pure product patent, defining the claimed invention "in terms of structural characteristics only." *See* 3-8 *Chisum on Patents* § 8.05 (Lexis 2013). Unlike the '343 patent, the asserted claims in the '727 patent do not require the use of "efficient mixing" in manufacturing the claimed bivalirudin drug product.

Based on these holdings, both sides now seek to exclude their opponent from introducing expert opinions or other evidence at trial regarding "efficient" and "inefficient" mixing conditions. Defendants argue that the Court should preclude TMC's experts from offering or relying on the opinion that Mylan's ANDA prescribes an "efficient mixing" process. Defendants contend that because the Court has already decided that Mylan's ANDA does not use "efficient mixing," these opinions will not assist the trier of fact.

TMC, for its part, argues that the Court should preclude Defendants from offering any evidence of "efficient" or "inefficient" mixing because the Court has decided that the asserted claims in the '727 patent—the only patent still at issue in this case—do not contain an "efficient mixing" or other type of process limitation. TMC argues that only the structural characteristics of the claimed invention and the accused product—*i.e.*, its impurity levels, reconstitution time, pH level, etc.—are relevant, not the compounding process used to create the product.

LEGAL STANDARD

I. *Daubert* Standard

"The admissibility of expert testimony is governed by Federal Rule of Evidence 702 and the Supreme Court's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 113 S. Ct. 2786, 125 L. Ed. 2d 469 (1993)." *Lewis v. Citgo Petroleum Corp.*, 561 F.3d 698, 705 (7th Cir. 2009). Rule 702 provides, in relevant part, that "[i]f scientific, technical or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training or education, may testify thereto in the form of an opinion . . . ." *Id.* *See also Happel v. Walmart Stores, Inc.*, 602 F.3d 820, 824 (7th Cir. 2010).

Under the expert-testimony framework, courts perform the gatekeeping function of determining whether the expert testimony is both relevant and reliable prior to its admission at trial. *See id.*; *Power Integrations, Inc. v. Fairchild Semiconductor Int'l., Inc.*, 711 F.3d 1348, 1373 (Fed. Cir. 2013); *see also Apple Inc. v. Motorola, Inc.*, --- F.3d ----, 2014 WL 1646435, at *18-19 (Fed. Cir. Apr. 25, 2014). In doing so, courts "make the following inquiries before admitting expert testimony: first, the expert must be qualified as an expert by knowledge, skill, experience, training, or education; second, the proposed expert must assist the trier of fact in

determining a relevant fact at issue in the case; third, the expert's testimony must be based on sufficient facts or data and reliable principles and methods; and fourth, the expert must have reliably applied the principles and methods to the facts of the case." *Lees v. Carthage College*, 714 F.3d 516, 521-22 (7th Cir. 2013); *see also Stollings v. Ryobi Tech., Inc.*, 725 F.3d 753, 765 (7th Cir. 2013); *Power Integrations*, 711 F.3d at 1373.

"*Daubert* instructs that expert testimony must be relevant and factually linked to the case in order to meet Rule 702's 'helpfulness' requirement." *United States v. Gallardo,* 497 F.3d 727, 734 (7th Cir. 2007) (citing *Daubert,* 509 U.S. at 591, 113 S. Ct. 2786, 125 L. Ed. 2d 469). Expert testimony that does not relate to any issue in the case "is not relevant and, ergo, non-helpful." *Daubert,* 509 U.S. at 591, 113 S. Ct. 2786, 125 L. Ed. 2d 469. Because the rule permitting expert testimony is liberal, however, "[a]bsent strong factors favoring exclusion, 'doubts regarding whether an expert's testimony will be useful should generally be resolved in favor of admissibility.'" *Davis v. Duran,* 276 F.R.D. 227, 232 (N.D. Ill. 2011).

II. Motion *in Limine* Standard

Although the Federal Rules of Evidence do not explicitly authorize *in limine* rulings, the practice has developed pursuant to the district court's inherent authority to manage the course of trials. *Luce v. United States,* 469 U.S. 38, 41 n. 4, 105 S.Ct. 460, 83 L.Ed.2d 443 (1984). *In limine* rulings avoid delay and allow the parties the opportunity to prepare themselves and witnesses for the introduction or exclusion of the applicable evidence. *See Wilson v. Williams,* 182 F.3d 562, 566 (7th Cir. 1999); *United States v. Connelly,* 874 F.2d 412, 416 (7th Cir. 1989). The Court will only grant a motion *in limine* when the evidence is clearly inadmissible for any purpose. *See Jonasson v. Lutheran Child & Family Servs.,* 115 F.3d 436, 440 (7th Cir. 1997); *Betts v. City of Chicago, Illinois,* 784 F.Supp.2d 1020, 1023 (N. D. Ill. 2011).

Trial courts have broad discretion in ruling on evidentiary issues before trial. *See Christmas v. City of Chi.,* 682 F.3d 632, 640 (7th Cir. 2012). If the *in limine* procedural environment makes it too difficult to evaluate an evidentiary issue, the Court may defer ruling on the motion until trial. *See Jonasson*, 115 F.3d at 440. Moreover, regardless of the Court's initial ruling on a motion *in limine,* the Court may alter its ruling during the course of trial. *See Empire Bucket, Inc. v. Contractors Cargo Co.,* 739 F.3d 1068, 1071 n.3 (7th Cir. 2014); *Farfaras v. Citizens Bank & Tr. of Chi.,* 433 F.3d 558, 565 (7th Cir. 2006). "These limiting principles apply in all trial settings, but they have even greater force in a bench trial, because the trial judge has flexibility to provisionally admit testimony or evidence and then discount or disregard it if upon further reflection it is entitled to little weight or should not have been admitted at all." *Bone Care Int'l., LLC v. Pentech Pharma., Inc.,* No. 08-cv-10832010 WL 3894444, at *1 (N.D. Ill. Sept. 30, 2010); *see also SmithKlineBeecham Corp. v. Apotex, Corp.,* 247 F. Supp. 2d 1011, 1042 (N.D. Ill. 2003) (Posner, J.) ("In a bench trial it is an acceptable alternative to admit evidence of borderline admissibility and give it the (slight) weight to which it is entitled."), *vacated upon rehearing en banc and aff'd on other grounds,* 403 F.3d 1331 (Fed. Cir. 2005).

In the present motion *in limine*, TMC argues that the Court should preclude Defendants from putting on evidence regarding the use of "efficient" or "inefficient" mixing conditions because, in light of the Court's ruling that the '727 patent does not contain any process limitations, this evidence is irrelevant. (*See* TMC Mot. at 1-2.) Under Federal Rule of Evidence 402, evidence is relevant if "it has any tendency to make a fact more or less probably than it would be without the evidence" and "the fact is of consequence in determining the action." Fed. R. Evid. 401(a)-(b).

ANALYSIS

I. Defendants' *Daubert* Motion

Defendants seek to preclude TMC's chemistry expert, Dr. Klibanov, from opining at trial that Mylan's ANDA prescribes an "efficient mixing" process and TMC's statistical expert, Dr. Salzberg, from offering opinions based on Dr. Klibanov's purportedly precluded opinions. (*See* Defs. Mem. at 1.) Specifically, Defendants move to exclude the opinions found in paragraphs 119-132 of Dr. Klibanov's opening report; paragraphs 32-33, 43-54, 58, 60-66, and 76 of his reply report; and Section III.A of Dr. Salzberg's report. (*Id.* at 6, 10.)

TMC acknowledges that the Court's rulings on summary judgment foreclose some of Dr. Klibanov's opinions. TMC represents that Dr. Klibanov does not intend to offer those opinions at trial. (*See* TMC Resp. Br. at 1 ("[T]o the extent the Court has ruled on the issues in this case, [TMC] and its experts will not attempt to reargue those issues at trial. Dr. Klibanov submitted his reports prior to the Court's summary judgment opinion and, contrary to Mylan's assertions, does not intend to testify that 'Mylan's process is efficient.'").) Accordingly, the Court denies Defendants' motion as moot with respect to paragraphs 119-132 of Dr. Klibanov's opening report and paragraphs 32-33, 43-54, 58, and 60-66 of his reply report. The only remaining dispute is whether the Court's summary judgment rulings preclude Dr. Klibanov from offering the opinion in paragraph 76 of his reply report and Dr. Salzberg from offering opinions that rely on paragraph 76 of Dr. Klibanov's report. (*See* Defs. Reply Br. at 1.)

In paragraph 76 of his reply report (*see* R. 362-3, Greb Decl. Ex. 7, Klibanov Reply Rep.), Dr. Klibanov opines:

> [T]he minimized Asp^9 values for both the drug substance and drug product (*i.e.*, the insubstantial generation of the Asp^9 impurity during the compounding process) confirm that Mylan employed efficient mixing in preparing its Generic Bivalirudin. Ex. 25, MYL0000428; Ex. 18 at MYL0001922. The Asp^9 levels of

> the active pharmaceutical ingredient (API) bivalirudin were 0.08% and 0.03% for β-Asp^9 and α-Asp^9, respectively. Ex. 25 at MYL0000428. The sum of β-Asp^9 and α-Asp^9 in the API is thus 0.11%. Mylan's Certificate of Analysis for its exhibit batch states that the Asp^9 levels in the drug product were 0.084% and 0.11% for β-Asp^9 and α-Asp^9, respectively. Ex. 18 at MYL0001922. The sum of Asp^9 in the drug product is thus 0.194%. That the Asp^9 values of the API and of the drug product are comparable and differ by as little as 0.084% (0.194% - 0.11%) reveals that Mylan did not generate significant amounts of Asp^9 during the compounding process and hence used efficient mixing to prepare its Generic Bivalirudin. Therefore, I see no reason to expect significant variability in future batches of Mylan's Generic Bivalirudin.

(*Id.* ¶ 76.) Defendants argue that Dr. Klibanov's opinion there is "no reason to expect significant variability in future batches of Mylan's Generic Bivalirudin" depends on Dr. Klibanov's conclusion that Mylan's ANDA process used "efficient mixing"—a conclusion that the Court specifically rejected on summary judgment. (Defs. Mem. at 8-9.) According to Defendants, Dr. Klibanov's opinion is therefore irrelevant and unhelpful to the trier of fact. (*Id.*; *see also* Defs. Reply Br. at 2-3.) The Court disagrees.

Although Dr. Klibanov's opinion expressed in the first and penultimate sentences of paragraph 76 that Mylan used "efficient mixing" to prepare its bivalirudin drug product contradict the Court's summary judgment ruling, the remainder of Dr. Klibanov's opinion in paragraph 76 does not. Dr. Klibanov couches his opinion in terms of "efficient mixing," but beyond that label, paragraph 76 stands for the unremarkable position that because the compounding process Mylan used to produce its exhibit batch generated such small amounts of Asp^9 impurities (0.084%), there is no reason to expect that the same process would generate significantly greater impurities in the future. This conclusion does not conflict with the Court's summary judgment ruling that the mixing conditions Mylan's ANDA process uses are more inefficient than the conditions described in Example 4 of the patent specification. That ruling was based on the characteristics of those mixing conditions, not the amount of impurities the conditions generated.

Defendants, of course, may argue that there is a reason to expect that Mylan's compounding process, if repeated, would generate significantly greater impurities, *i.e.,* because it does not practice "efficient mixing." Defendants are free to raise this argument at trial and vigorously cross-examine Dr. Klibanov on this issue. That argument, however, does not make Dr. Klibanov's observation that Mylan's compounding process generated only trace amounts of Asp^9 impurities in Mylan's exhibit batch any less relevant to determining whether Mylan's bivalirudin drug product will infringe the '727 patent's product claims. The asserted claims in the '727 patent require, among other things, that the pharmaceutical batches of bivalirudin contain a maximum level of Asp^9 impurities of about 0.6% or less. The amount of impurities Mylan's compounding process generated in producing its exhibit batch is certainly relevant to determining if Mylan's bivalirudin drug product will meet that limitation.

Indeed, as Defendants acknowledge, although the compounding process Mylan uses is not directly relevant to infringement because the asserted claims in the '727 patent do not contain process limitations, the process is still indirectly relevant to infringement because the amount of impurities generated during that process will affect whether Mylan's bivalirudin drug product will infringe the maximum Asp^9 impurities limitation of the asserted claims. (*See* TMC Resp. Br. at 1 ("[T]o the extent the Court has ruled on the issues in this case, [TMC] and its experts will not attempt to reargue those issues at trial. Dr. Klibanov submitted his reports prior to the Court's summary judgment opinion and, contrary to Mylan's assertions, does not intend to testify that 'Mylan's process is efficient.'").) Accordingly, even though Dr. Klibanov cannot opine whether Mylan's compounding process is "efficient" under the patent, he can, however, opine regarding how Mylan's process (regardless of whether the patent deems it "efficient" or not) will affect the characteristics of the bivalirudin drug product it generates.

Finally, the Court notes that the risk of confusion or prejudice from allowing Dr. Klibanov to offer the opinion at issue is lessened where, as here, trial is before the Court, not a jury. *See In re Salem,* 465 F.3d 767, 777 (7th Cir. 2006) ("[W]here the factfinder and the gatekeeper are the same, the court does not err in admitting the evidence subject to the ability later to exclude it or disregard it if it turns out not to meet the standard of reliability established by Rule 702."); *Metavente Corp. v. Emigrant Sav. Bank,* 619 F.3d 748, 760 (7th Cir. 2010) (observing that "the court in a bench trial need not make reliability determinations before evidence is presented" because "the usual concerns of the rule—keeping unreliable expert testimony from the jury—are not present in such a setting."). For these reasons, the Court denies Defendants' motion to exclude Dr. Klibanov's opinion in paragraph 76 in large part, but grants it with respect to the statements in the first and second-to-last sentences opining that Mylan's compounding process uses "efficient mixing." Furthermore, because Defendants' only challenge to Dr. Salzberg's opinions was that he had relied on Dr. Klibanov's statement that he "[saw] no reason to expect significant variability in future batches of Mylan's Generic Bivalirudin," the Court also denies Defendants' motion to exclude Dr. Salzberg's challenged opinions.

II. TMC's Motion *in Limine*

TMC seeks to exclude Defendants' expert, Dr. David Auslander, from offering the opinions contained in paragraphs 23, 27, 120-34, 139-43, 149, 153 and 164 of his opening report; paragraphs 21-24, 26, 29-43, and 53 of his response report; and paragraphs 8, 26, 33-37, 43-44, 46-48, 55-57, 62, 68-74, 76, 78, 80, 110-11 of his reply report. (*See* TMC Mot. at 5, 8.) TMC also seeks to exclude Defendants' statistical expert, Dr. Ian McKeague from offering the opinions contained in paragraphs 38-46 of his expert report (*see id.* at 8-9), and prevent Defendants' fact witnesses from testifying regarding efficient or inefficient mixing. (*See id.* at 9-10.)

Defendants acknowledge that several of Dr. Auslander's opinions that Defendants seek to exclude contradict the Court's ruling on summary judgment that the asserted claims in the '727 patent do not incorporate an "efficient mixing" limitation, (*see* Defs. Resp. Br. at 3-4, 8 n.4, 11 n.7, 12; *see also id.* at App'x A), and they represent that they will not offer at trial any opinions that contradict the Court's ruling. (*See id.*) Based on this representation, the Court denies TMC's motion *in limine* as moot with respect to paragraphs 23, 27, 139-143, 149, 153, and 164 of Dr. Auslander's opening report; paragraphs 21, 23-24, 29-43 of his response report; and paragraphs 8, 26, 33-37, 74, 76, 78, 80, 110, and 110 of his reply report. (*See id.* at App'x A.) The Court now turns to the opinions in dispute.

First, the Court disagrees with TMC's contention that because the '727 patent claims lack an "efficient mixing" limitation, opinions concerning the efficiency of Mylan's compounding process "do not relate to any element of the claims of the '727 patent." (*See* TMC Reply Br. at 2.) Although the '727 patent does not require the use of "efficient mixing," the inefficiency of Mylan's mixing conditions is relevant to determining whether its proposed bivalirudin drug product will meet the maximum Asp^9 impurity limitation in the asserted claims. Mylan cites evidence indicating a nexus between the efficiency of the mixing conditions used during the compounding process and the level of Asp^9 impurities present in the final drug product. (*See* Mylan Resp. Br. at 4-7.) Furthermore, the Asp^9 impurity levels TMC's in Original Angiomax® product, which was manufactured using "inefficient mixing" conditions, may help predict the likely Asp^9 impurity levels in Mylan's proposed bivalirudin drug product, which is also manufactured using "inefficient mixing" conditions.

This evidence certainly meets the Federal Rules' relevancy standard, *see* Fed. R. Evid. 401; whether it ultimately carries the day, on the other hand, is a question for trial. Accordingly,

the Court denies TMC's motion *in limine* with respect to paragraphs 22, 26 and 53 of Dr. Auslander's response report and paragraphs 38-46 of Dr. McKeague's report. Those opinions bear on the correlation "inefficient mixing" conditions have to the level of Asp^9 impurities present in the final bivalirudin drug product. They are therefore relevant to determining whether Mylan's proposed bivalirudin drug product, which is generated using "inefficient mixing" conditions, meets the maximum Asp^9 impurity levels recited in the '727 patent.

Second, the Court agrees with Mylan that evidence regarding "efficient mixing" conditions is relevant to Mylan's obviousness argument. "In order to render a claimed apparatus or method obvious, the prior art as a whole must enable one skilled in the art to make and use the apparatus or method." *Beckman Instruments, Inc. v. LKB Produkter AB,* 892 F.2d 1547, 1551 (Fed. Cir. 1989); *see also Therasense, Inc. v. Becton, Dickinson & Co.,* 593 F.3d 1289, 1297 (Fed. Cir. 2010), *vacated for rehearing en banc on inequitable conduct,* 374 Fed. App'x 35 (Fed. Cir. 2010). The benefit of having a drug product with fewer impurities than its predecessor is clear; the difficulty is in determining how to create a more pure drug. Accordingly, for Defendants to succeed on their obviousness claim, they need to prove not only that creating a bivalirudin drug product with lower impurity levels was obvious to one skilled in the art, but also that the *method* for doing so was obvious to one skilled in the art. *See Beckman Instruments,* 892 F.2d at 1551; *Therasense,* 593 F.3d at 1297. Defendants' evidence purportedly showing that the prior art as a whole suggested the use of "efficient mixing" as an obvious way to generate the claimed product in the '727 patent is therefore relevant to the obviousness of the asserted claims.

TMC argues that the Court should exclude this evidence because the '727 patent does not contain an "efficient mixing" condition. As explained above, however, the patent specification and other evidence Mylan cites suggest that the "efficient mixing" and low amounts of Asp^9

impurity levels in the resulting drug product go hand-in-hand. Thus, the obviousness of "efficient mixing" may directly correspond to the obviousness of the bivalirudin drug product claimed in the '727 patent. Furthermore, because the trial is a bench trial, the Court has flexibility to provisionally admit this evidence and then discount or disregard it if upon further reflection the evidence is entitled to little weight or should not have been admitted at all. *See Bone Care Int'l., LLC,* 2010 WL 3894444, at *1; *see also SmithKlineBeecham Corp,* 247 F. Supp. 2d at 1042. For these reasons, the Court denies TMC's motion to exclude paragraphs 120-22 and 123-34 of Dr. Auslander's opening report and paragraphs 43-44, 46-48, 55-57, 62, and 68-73 of his reply report.

Finally, with respect to TMC's motion to exclude the testimony of fact witnesses regarding "efficient mixing," TMC has not identified any particular testimony to which it objects that is not covered by (1) Defendants' representation that it will not offer testimony at trial contradicting the Court's summary judgment ruling that the '727 patent claims do not contain an "efficient mixing" limitation (*see* Defs. Resp. Br. at 12), or (2) the Court's holding that evidence regarding the inefficiency of Mylan's compounding process is relevant to determining whether Mylan's proposed bivalirudin drug product will infringe the maximum Asp^9 impurity limitation in the asserted claims. The Court, therefore, denies this portion of TMC's motion. TMC may raise objections to specific testimony at trial, at which time the Court will rule based on the substance of the testimony at issue.

CONCLUSION

For the foregoing reasons, the Court grants Defendants' *Daubert* motion in part, denies it part, and denies it as moot in part, and it denies TMC's motion *in limine* in part and denies it as moot in part.

Dated: May 15, 2014

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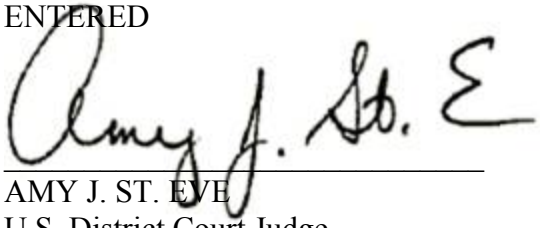

AMY J. ST. EVE
U.S. District Court Judge